though the mechanism of TDI-induced asthma is unclear, its clinical presentation often suggests that "sensitization" occurs. Cases of hypersensitivity pneumonitis associated with TDI exposure also have been reported. Toluene diisocyanate is a mucosal irritant in higher concentrations, and workers who have had exposure to it who do not appear to be "sensitized" have had accelerated annual rates of decline in ventilatory function. Nonspecific airway hyperresponsiveness has been induced in guinea pigs after single, short-term exposures to TDI at a concentration of 3 parts per million, suggesting that immunologic sensitization is not the only etiologic factor.

Contrary to the usual conception of occupational asthma, a persistence of asthmatic symptoms and nonspecific airway hyperresponsiveness after exposure ceases appears to be the norm rather than the exception with TDI-induced asthma. Many studies have confirmed this alarming potential of TDI exposure. Because the duration of asthmatic symptoms before diagnosis is associated with persisting symptoms after the cessation of exposure, there is a need for prompt diagnosis and the removal of affected workers.

Because of the health risks associated with TDI exposure, other diisocyanate compounds have been used in the manufacture of polyurethane paints and coatings. In particular, hexamethylene diisocyanate is popular in automotive spray-painting applications. It is alleged by paint manufacturers that hexamethylene diisocyanate is a less potent asthma-inducer than TDI, but case reports of asthma and hypersensitivity pneumonitis induced by this compound make this questionable.

In an effort to reduce exposure to "free" diisocyanate monomers in spray painting, manufacturers have developed paints consisting primarily of polyisocyanates ("prepolymers"). Although measured diisocyanate exposure in spray-painting areas may be reduced by the use of prepolymerized paints, it is not clear that such paints are completely without asthma-inducing potential. Our experience is that cases of occupational asthma due to the use of prepolymerized polyurethane spray paints do occur.

It is prudent to advise employers to provide, and workers to wear, appropriate respiratory protective gear in polyurethane spray-painting areas even if diisocyanate levels have been measured to be below the threshold limit value. It is not at all clear that the current threshold limit value will prevent the development of asthma.

Clinicians can also participate in the solution of this problem by identifying one of the isocyanates as the cause of adult-onset asthma. The immediate removal of the affected person from the work setting is likely to be an important factor in the prognosis.

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Health Hazards of Occupational Diesel Exhaust Exposure

DIESEL ENGINES generate 50 to 100 times more particulates than do gasoline engines, and the organic extracts of diesel exhaust have been known since the 1950s to be carcinogenic in rodents. In the late 1970s the gasoline shortages and increasing number of light-duty diesel vehicles resulted in a heightened concern about the adverse health effects of diesel exhaust exposure. Since then numerous laboratory and epidemiologic studies have been completed addressing this issue.

Studies in the United States, Germany, and Japan have shown significant increases in lung tumors among rats with long-term exposure to high concentrations of diesel exhaust. Diesel exhaust carcinogenicity is both dose- and time-related. The mechanism of diesel carcinogenicity is thought to be the interaction of organic chemicals, particularly polycyclic aromatic hydrocarbons associated with diesel exhaust soot, with lung DNA. This is supported by recent studies showing higher levels of DNA adducts in the peripheral lung tissues of exposed rats, which is the location of diesel exhaust-induced lung tumors.

Diesel engines came into common industrial use in the 1940s and 1950s. Early epidemiologic studies were limited by inadequate latency times among exposed populations and poor estimates of diesel exposure. Many studies have also been limited by sample sizes too small to detect a small increase in lung cancer risk. Recent studies have addressed these limitations more adequately and have included populations with adequate sample sizes. An extensive series of studies among railroad workers in the United States found consistent evidence of a small but significant increase in lung cancer risk among current and former workers. For workers younger than 65 years with 20 years or more of exposure, the relative risk for lung cancer was approximately 1.3 to 1.4 compared with that of workers without such exposure. Studies among Canadian railroad workers and US truck drivers have had similar findings.

The laboratory and epidemiologic studies have resulted in the International Agency for Research on Cancer (IARC) recently concluding that there was sufficient evidence for carcinogenicity in animals of whole diesel engine exhaust and diesel engine exhaust particles. The IARC also concluded that there was limited evidence for carcinogenicity of diesel engine exhaust in humans. The risk from lifetime occupational exposure is small but biologically plausible and consistent with epidemiologic data. Populations at risk include persons whose occupations involve work in close proximity to operating diesel engines, such as railroad, bus, truck, and heavy equipment repair personnel and possibly operators. The data are limited on the possible interaction of diesel exhaust with other known lung carcinogens, including cigarette smoking.

There are few studies on the nonmalignant respiratory effects of occupational diesel exhaust exposure. Studies of miners have found an increase in some respiratory tract symptoms associated with diesel exhaust exposure, but no definite changes in pulmonary function have been found. Preliminary results of a mortality study have suggested that lifetime diesel exposure may be associated with increased

chronic obstructive pulmonary disease mortality. More work is needed on the possible nonmalignant effects of workplace exposure to diesel exhaust.

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Health Hazards of Radon Exposure

RADON, A CAUSE of lung cancer in miners of uranium and other underground minerals, has become recognized as a potentially important cause of lung cancer in the general population. This naturally occurring gaseous member of the uranium 238 decay series decays into a series of solid, short-lived isotopes referred to as radon daughters, progeny, or decay products. The release of α-particles by inhaled radon decay products is presumed to damage cells of the bronchial epithelium and thereby cause lung cancer.

As data on indoor air quality have accumulated, it has become apparent that radon and its decay products are present in indoor environments and at unacceptably high concentrations in some homes and other structures. Because the uranium-decay series is present in virtually all rocks and soils, radon contaminates the soil gas that passes into indoor and outdoor air. Thus in homes, the principal source of radon is the soil beneath the home, but building materials, water used in the home, and utility natural gas may also contribute. Measurements made in the United States indicate that the distribution of radon levels in houses is skewed, with the average at about 1.5 pCi per liter, but with many homes in the distribution's tail having much higher levels.

From animal and epidemiologic data, we have a sound understanding of some aspects of radon carcinogenesis. The lung cancer risk has been shown to increase with increasing exposure; the preponderance of the epidemiologic evidence indicates a synergism between cigarette smoking and radon exposure. The epidemiologic studies of underground miners provide the data needed to project the lung cancer risk of indoor exposure to radon. Computer models of the dosimetry of radon decay products in the lungs indicate a comparable potency of radon as a carcinogen with exposures in homes and in mines.

Although substantial uncertainty remains concerning the lung cancer risk associated with indoor radon, all projections indicate that the problem is substantial. Because carcinogenesis by radon is considered to follow a no-threshold exposure-response relation, any exposure, even the average for the population, conveys some risk. Remarkably high risks of lung cancer are projected for high exposures. For the US population, estimates of the annual number of lung cancer cases attributable to radon range from about 5,000 to 20,000 cases.

Health care providers should be prepared to advise patients concerning the risks of indoor radon and not dismiss the problem. Following the 1988 advisory of the Environmental Protection Agency (EPA), the measurement of radon in homes should be advocated. We lack other methods for identifying homes with unacceptable concentrations. Longer term measurements, rather than shorter term measurements with a charcoal canister, are preferred under most circumstances. The results of measurements should be interpreted cautiously, but mitigation should be advised for homes with high levels. The EPA's guidelines offer one framework for interpreting measurements, but the highest acceptable level—4 pCi per liter—is not a boundary between safe and unsafe levels. Smokers should be cautioned about the synergism between smoking and radon exposure and advised to stop smoking.

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Male Reproductive Toxicity

WORK-RELATED BIRTH DISORDERS are commonly regarded as related to the occupational experiences of pregnant women. Evidence suggests, however, that toxic exposures in men can also influence reproduction. There are many theoretic mechanisms by which this might occur: a pregnant woman might have direct exposure to a toxin inadvertently transported home from the workplace; a systemic, endocrine, or testicular toxic reaction could impair the male libido or fertility; and systemically absorbed chemicals that cross the blood-testis barrier or are secreted into seminal fluids might either damage sperm or directly affect a fetus or oocyte through sexual transmission.

A number of workplace chemicals have been reported to cause sperm abnormalities. Lead exposure, for example, has been shown in a study of 150 male storage battery workers to be dose-related to the prevalence of oligospermia, sperm hypomotility, and abnormal sperm characteristics. Exposures to boron, cadmium, manganese, and mercury have each been linked to sperm abnormalities, but these data come from small studies or case reports and are inconclusive. Abnormal spermatogenesis has also been described in epidemiologic studies of men with exposure to certain organic compounds, including carbon disulfide, chloroprene, dinitrotoluene and toluene diamine, and the pesticides carbaryl, chlordecone, and dibromochloropropane (DBCP). In many instances these sperm abnormalities have been of indeterminate clinical significance, but human exposures to lead and to DBCP have produced infertility, and the more severe cases of DBCP spermatotoxicity have been irreversible. There is generally minimal information from studies in humans or animals with which to judge the potential spermatotoxicity of the thousands of other commonly used industrial chemicals.

Many authorities question whether paternal chemical exposures can influence a partner's pregnancy outcome or cause abnormalities that are transmissible to offspring, but there is evidence that such adverse effects occur. Paternal exposures to lead, chloroprene, and DBCP have each been reported to increase rates of spontaneous abortion. Other epidemiologic studies have also suggested, for example, that partners of male anesthetists and of copper smelter workers are at risk for spontaneous fetal loss and that paternal "hydrocarbon" exposure may increase the occurrence of low birth weight, central nervous system malformations, and childhood cancers. Although few human studies have been confirmed with subsequent studies, they are supported in principle by the findings of animal research in which exposures of male animals to various alkylating agents have subsequently produced genetic mutations, chromosomal translo-